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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/770,943	01/25/2001	Eyal Raz	UCSD-173CON	8209

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EXAMINER	
DUFFY, PATRICIA ANN	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
09/04/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.**	**Applicant(s)**	
	09/770,943	RAZ ET AL.	
	Examiner	**Art Unit**	
	Patricia A. Duffy	1645	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED _____ FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *17 August 2009*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *32-36,38 and 39*.
   Claim(s) withdrawn from consideration: *45*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☒ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). 7-14-09
13. ☐ Other: _____.

/Patricia A. Duffy/
Primary Examiner, Art Unit 1645

Continuation of 11. does NOT place the application in condition for allowance because: Applicants point to the specification indicating that administration of IIS reduce the level of specific cytokines and shift the type of immune response. The specification teaches that specific IIS reduce specific cytokines in vitro. The specification does not provide any evidence of a reduce immune respone in a primed animal with the combination of a conjugate of the IIS and autoantigen. The presence of the autoantigen in the conjugate must be considered. In a person having autoimmune disease the immune system is primed to respond to autoantigen. The specification does not teach that the IIS-autoantigen conjugate has the effect of reducing the cytokines or in the treatment of autoimmune disease as contemplated by the specification. The examples drawn to inhibiton of proliferation of mouse splenocytes does not use the claimed conjugate and the splenocytes are not from an animal having autoimmune disease. The in vivo miliu of autoimmune disease is complicated. The conjugate contains two parts, one of which is the autoantigen itself. The use of autoantigens in treatment of autoimmune diseases is replete with failures. The conclusion that because the IIS is inhibitory to ISS_induced proliferation in splenocytes ignores the situation in vivo where one skilled in the art would expect that the autoantigen component of the conjugate would be immune stimulatory and may exacerbate disease and the ISS and autoantigen work by completely different mechanisms. Therfore, example 1 of the specification does not provide evidence of enablment of the claimed invention for treatment of autoimmune disease. As previously indicated induction of a Th2 response does not indicate that the autoimmune disease is treated, because the Th2 response also produces antibodies. These antibodies could exacerbate the ongoing autoimmune response as would the Th1 antibodies. The concept of immune deviation was addressed fully on this record and is not persuasive to support pharmaceutical compositions as claimed. Applicats argue that the conjugate would be reasonably expected to be effective as the IIS alone. This is not persuasive is amounts to attorney argument in the absence of evidence to support the conclusion. There is no evidence that the IIS-conjugate is effective in vitro or in vivo to ameloriate an autoimmune response. Applicants argue that the references drawn to autoantigens are irrelevant to the claims since the claims are drawn to conjugates. This is not persuasive, Applicants cannot ignore the body of evidence that speaks to one of the active components of the conjugate. When the conjugate has two active components, that can act in contadictory manners according to the art, one simple cannot predict how the conjugate will function in a patient having autoimmune disease. The art of record inidcates the difficulties in immune-related treatment of autoimmune disease at the time of the invention. The majority of the arguments presented argue functionality of the IIS in the absence of an ongoing autoimmune disease. As such, the in vitro models are not art accepted models for being reaonalby predictive of treatment of autoimmune disease in vivo. The post filing evidence again argued does not establish enablment for the claimed invention and does not establishe enablement at the time of the claimed invention. The claimed composition was not tested in any in vitro or in vivo model reasonably predictive of therapy. The argued art does not read on the claimed invention. Applicants argue the IIS component and do not establishe that the art meets the structural limitation of the claims and therefore does not establish with post filing evidence enablment at the time of the invention for the claimed invention. Applicants argue that the Th2 response can be used to treat autoimmune disease. This is not persuasive because the specificaiton as filed does not establish that a Th2 response can be modulated in the presence of a ongoing Th1 response with the claimed conjugate. Furthermore it is well established in the ar that the EAE mouse model is not predictive of multiple sclerosis therapy. The art also state shtthe therapeutic manipulation of the Th1/Th2 response is inherently dangerous and unpredictable. Applicants have not demonstrated that the claimed conjugate is effective in vivo for immune deviation and that such deviation is therapeutic. Augments and evidence not drawn to the efficacy of the claimed invention is not persuasive in view of the body of evidence of record that establishes the unpredictabilty of treatment of autoimmune disease, the lack of in vitro and/or in vivo data correlating the conjugate in a relevant in vitro or in vivo model with therapeutic efficacy for the claimed conjugate. The rejection is maintained for all the reasons made of record..